2D01

Access DB# 92667

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: K. Weddington Examiner # : 68082 Date: 4-28-03
Art Unit: 1614 Phone Number 30 8-4650 Serial Number: 09/926,807
Mail Box and Bldg/Room Location: CM1-2D17 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Jacobus Johannes Marion Meyer; Namrita Lall

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

A method of treating tuberculosis with formula I

RECEIVED
APR 28 2003
TECHNOLOGY CENTER 1600

****

STAFF USE ONLY

Searcher: Sheppard
Searcher Phone #: 308-4444
Searcher Location: _____
Date Searcher Picked Up: _____
Date Completed: 4/30/03
Searcher Prep & Review Time: _____
Clerical Prep Time: _____
Online Time: _____

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN _____
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

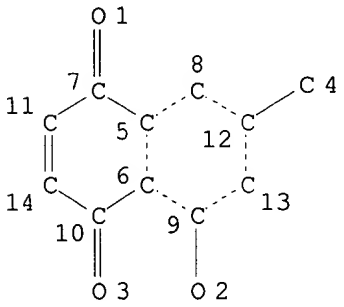
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:45:32 ON 30 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Apr 2003 VOL 138 ISS 18
FILE LAST UPDATED: 29 Apr 2003 (20030429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=>

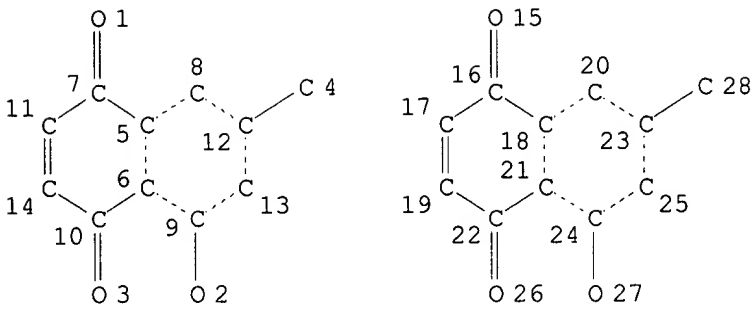
=> d stat que
L24 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L25 875 SEA FILE=REGISTRY SSS FUL L24
L26 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L27 112 SEA FILE=REGISTRY SUB=L25 SSS FUL L26
L28 160 SEA FILE=HCAPLUS ABB=ON PLU=ON L27
L29 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND ?TUBERCUL?

=>
=>

=> d ibib abs hitrn l29 1-2

L29 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:794683 HCAPLUS
DOCUMENT NUMBER: 137:75724
TITLE: Inhibition of drug-sensitive and drug-resistant strains of Mycobacterium **tuberculosis** by diospyrin, isolated from Euclea natalensis
AUTHOR(S): Lall, N.; Meyer, J. J. M.
CORPORATE SOURCE: Department of Botany, University of Pretoria, Pretoria, 0002, S. Afr.
SOURCE: Journal of Ethnopharmacology (2001), 78(2-3), 213-216
CODEN: JOETD7; ISSN: 0378-8741
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binaphthoquinoid, diospyrin, was isolated from Euclea natalensis A.DC., and evaluated for its activity against drug-sensitive and drug-resistant strains of Mycobacterium **tuberculosis**. The minimal inhibitory concn. (MIC) of diospyrin was found to be 100 .mu.g/mL for all the M. **tuberculosis** strains.
IT **28164-57-0P**, Diospyrin
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** drug-sensitive and drug-resistant strains inhibition by Euclea natalensis isolate diospyrin)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:12397 HCAPLUS

DOCUMENT NUMBER: 134:68700
TITLE: Naphthoquinone derivatives and their use in the treatment and control of **tuberculosis**
INVENTOR(S): Meyer, Jacobus Johannes Marion; Lall, Namrita
PATENT ASSIGNEE(S): University of Pretoria, S. Afr.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000554	A2	20010104	WO 2000-IB837	20000622
WO 2001000554	A3	20010705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194137	A2	20020410	EP 2000-937123	20000622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: ZA 1999-4176 A 19990624
WO 2000-IB837 W 20000622

OTHER SOURCE(S): MARPAT 134:68700

AB Naphthoquinone derivs., or pharmaceutically acceptable salts thereof, are useful for the treatment and/or control of a **tuberculosis** caused by Mycobacterium **tuberculosis** in a patient. The naphthoquinone derivs. are administered orally, i.v., i.m., or transdermally. For example, diospyrin and 7-methyljuglone controlled effectively the sensitive and resistant strains of M. **tuberculosis** with min. inhibitory concn. (MIC) of 0.1 .mu.g/mL for diospyrin and 50 .mu.g/mL for 7-methyljuglone, while the MIC for the combination of two drugs was 10 .mu.g/mL.

IT **28164-57-0**, Diospyrin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(naphthoquinone derivs. and their use in control and treatment of **tuberculosis**)

=> select hit rn l29 1-2
E25 THROUGH E25 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 16:46:17 ON 30 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 APR 2003 HIGHEST RN 507441-92-1
DICTIONARY FILE UPDATES: 29 APR 2003 HIGHEST RN 507441-92-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

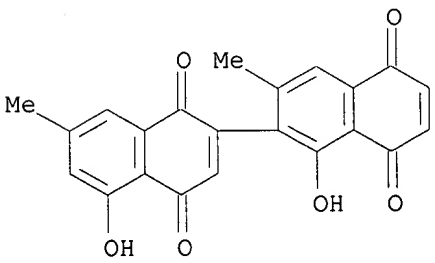
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=>

=> s e25
L30 1 28164-57-0/BI
(28164-57-0/RN)

=> d ide can l30 1

L30 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **28164-57-0** REGISTRY
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dihydroxy-3',7-dimethyl- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Diospyrin (7CI)
OTHER NAMES:
CN Euclein
FS 3D CONCORD
DR 27939-56-6
MF C22 H14 O6
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IPA, MEDLINE, NAPRALERT, RTECS*, SPECINFO, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

54 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
54 REFERENCES IN FILE CAPLUS (1957 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:251352

REFERENCE 2: 137:140377

REFERENCE 3: 137:75724

REFERENCE 4: 134:68700

REFERENCE 5: 133:168474

REFERENCE 6: 133:28470

REFERENCE 7: 133:17317

REFERENCE 8: 132:305640

REFERENCE 9: 132:134818

REFERENCE 10: 130:164730

```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:48:06 ON 30 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
```

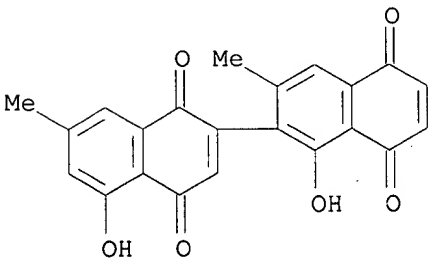


```
FILE COVERS 1907 - 30 Apr 2003  VOL 138 ISS 18
FILE LAST UPDATED: 29 Apr 2003  (20030429/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=>
=>

=> d stat que l32 nos
L24             STR
L25         875 SEA FILE=REGISTRY SSS FUL L24
L26             STR
L27         112 SEA FILE=REGISTRY SUB=L25 SSS FUL L26
L28         160 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27
L29           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND ?TUBERCUL?
L31           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28(L)(?MEDIC? OR ?PHARM? OR
                ?DRUG? OR THERAP? OR MYCOBACTERIUM)
L32           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 NOT L29


=>
=>

=> d ibib abs hitstr l32 1-3

L32  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2000:145304  HCAPLUS
DOCUMENT NUMBER:          132:305640
TITLE:                    Effects of atovaquone and diospyrin-based drugs on the
                          cellular ATP of Pneumocystis carinii f. sp. carinii
AUTHOR(S):                Cushion, Melanie T.; Collins, Margaret; Hazra,
                          Banasri; Kaneshiro, Edna S.
CORPORATE SOURCE:         Department of Internal Medicine, University of
                          Cincinnati College of Medicine, and Veterans Affairs
                          Medical Center, Cincinnati, OH, 45267-0560, USA
SOURCE:                   Antimicrobial Agents and Chemotherapy (2000), 44(3),
                          713-719
                          CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Atovaquone (also called Mepron, or 566C80) is a naphthoquinone used for
     the treatment of infections caused by pathogens such as Plasmodium spp.
```

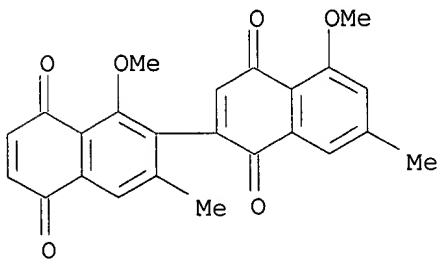
and Pneumocystis carinii. The mechanism of action against the malarial parasite is the inhibition of dihydroorotate dehydrogenase (DHOD), a consequence of blocking electron transport by the drug. As an analog of ubiquinone (coenzyme Q [CoQ]), atovaquone irreversibly binds to the mitochondrial cytochrome bc1 complex; thus, electrons are not able to pass from dehydrogenase enzymes via CoQ to cytochrome c. Since DHOD is a crit. enzyme in pyrimidine biosynthesis, and because the parasite cannot scavenge host pyrimidines, the drug is lethal to the organism. Oxygen consumption in P. carinii is inhibited by the drug; thus, electron transport has also been identified as the drug target in P. carinii. However, unlike Plasmodium DHOD, P. carinii DHOD is inhibited only at high atovaquone concns., suggesting that the organism may salvage host pyrimidines and that atovaquone exerts its primary effects on ATP biosynthesis. In the present study, the effect of atovaquone on ATP levels in P.carinii was measured directly from 1 to 6 h and then after 24, 48, and 72 h of exposure. The av. 50% inhibitory concn. after 24 to 72 h of exposure was 1.5 .mu.g/mL (4.2 .mu.M). The kinetics of ATP depletion were in contrast to those of another family of naphthoquinone compds., diospyrin and two of its derivs. Whereas atovaquone reduced ATP levels within 1 h of exposure, the diospyrins required at least 48 h. After 72 h, the diospyrins were able to decrease ATP levels of P. carinii at nanomolar concns. These data indicate that although naphthoquinones inhibit the electron transport chain, the mol. targets in a given organism are likely to be distinct among members of this class of compds.

IT **28164-57-0**, Diospyrin **39093-14-6**, Diospyrin dimethylether
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of atovaquone and diospyrin-based **drugs** on cellular ATP of Pneumocystis carinii)

RN 28164-57-0 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dihydroxy-3',7-dimethyl- (8CI, 9CI) (CA INDEX NAME)



RN 39093-14-6 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dimethoxy-3',7-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS

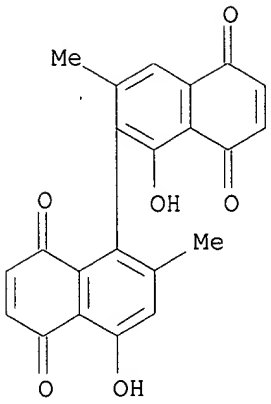
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:27367 HCAPLUS
DOCUMENT NUMBER: 128:162607
TITLE: Cell line-directed screening assay for inhibitors of thioredoxin reductase signaling as potential anti-cancer drugs
AUTHOR(S): Kunkel, Mark W.; Kirkpatrick, D. Lynn; Johnson, Jill I.; Powis, Garth
CORPORATE SOURCE: Arizona Cancer Center, University of Arizona Health Sciences Center, Tucson, AZ, 85724-5024, USA
SOURCE: Anti-Cancer Drug Design (1997), 12(8), 659-670
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have used a cell line-directed screening approach (CDSA) to identify novel inhibitors of the thioredoxin reductase signaling pathway which contributes to the transformed phenotype of some human tumors. Two 2-imidazolyl disulfide compds., previously identified as inhibitors of thioredoxin reductase, were screened for growth inhibitory activity in the National Cancer Institute (NCI) human cancer cell line panel. The COMPARE pattern recognition algorithm was used to identify similar compds. from >60,000 compds. in the NCI investigational drug database. Of 47 nondiscreet compds. tested in a thioredoxin reductase/thioredoxin insulin redn. assay, 37 (77%) were inhibitors with IC50s .ltoreq. 10 .mu.g/mL and 15 of those (32%) had IC50s .ltoreq. 1 .mu.g/mL. These compds. were all as selective or more selective for thioredoxin reductase than for glutathione reductase, while three compds. were inhibitors of thioredoxin. In comparison to CDSA, the no. of compds. with IC50s .ltoreq. 1 .mu.g/mL identified by screening of 52 compds. from the database whose growth inhibiting activity was unrelated to the activity of the disulfide compds. was only 2%. Screening of 221 randomly selected natural products gave only 3% of compds. with IC50s .ltoreq. 1 .mu.g/mL. Thus, the CDSA using data from the NCI cancer cell panel and known inhibitors of the selected target as seed compds. can greatly increase hit rates, compared with random screening, for identifying novel inhibitors of a target, in this case thioredoxin signaling.

IT **89475-33-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell line-directed screening assay for inhibitors of thioredoxin reductase signaling as potential anti-cancer **drugs**)

RN 89475-33-2 HCAPLUS
CN [1,2'-Binaphthalene]-5,5',8,8'-tetrone, 1',4-dihydroxy-2,3'-dimethyl- (9CI) (CA INDEX NAME)

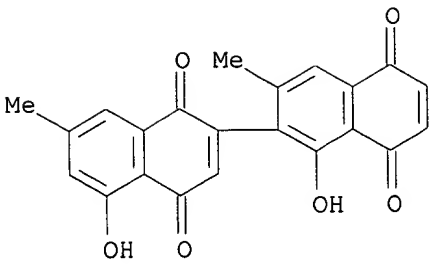


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

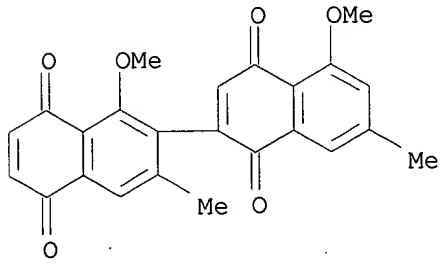
L32 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:542516 HCAPLUS
DOCUMENT NUMBER: 125:237771
TITLE: Pharmacological studies on the effect of the treatment of Swiss A mice with diospyrin, a tumor-inhibitory plant product, and its synthetic derivatives
AUTHOR(S): Pal, Sampa; Banerjee, Amalendu; Hazra, Banasri; Ray, Ratnamala; Bhattacharya, Dilip K.
CORPORATE SOURCE: Dep. Pharmacy Chem., Jadavpur Univ., Calcutta, 700 032, India
SOURCE: Phytotherapy Research (1996), 10(5), 393-397
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diospyrin, a bisnaphthoquinonoid plant product, and its derivs., have shown significant inhibitory activities against murine tumors in vivo. Studies on the hematol. status, serum protein and creatinine levels, activities of several serum glycolytic enzymes, and histopathol. of the mice inoculated with Ehrlich ascites carcinoma were carried out after treatment with diospyrin and four synthetic derivs. The prognostic significance of the pharmacol. parameters acting as markers of the diseased state was evident from these findings. Normal mice were also studied before and after treatment with these compds. which did not cause noticeable adverse effects on the vital parameters, thereby indicating the possibility of the utilization of diospyrin and derivs. as appropriate therapeutic agents.

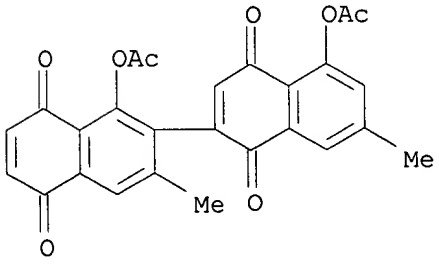
IT **28164-57-0**, Diospyrin **39093-14-6**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmacol.** studies on effect of treatment of Swiss A mice with antitumor agent diospyrin and synthetic derivs.)
RN 28164-57-0 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dihydroxy-3',7-dimethyl- (8CI, 9CI) (CA INDEX NAME)



RN 39093-14-6 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dimethoxy-3',7-dimethyl- (9CI) (CA INDEX NAME)

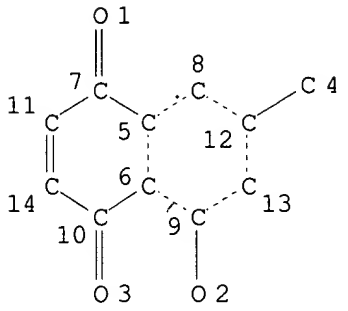


IT **60544-03-8**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmacol.** studies on effect of treatment of normal and tumor-bearing mice with antitumor agent diospyrin and synthetic derivs.)
RN 60544-03-8 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-bis(acetyloxy)-3',7-dimethyl- (9CI) (CA INDEX NAME)

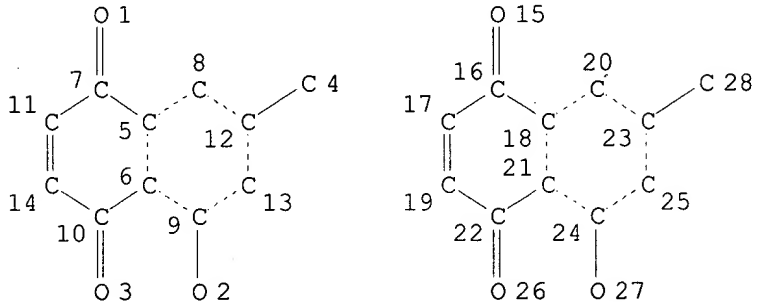


```
=> d stat que l36 nos
L24             STR
L25         875 SEA FILE=REGISTRY SSS FUL L24
L26             STR
L27         112 SEA FILE=REGISTRY SUB=L25 SSS FUL L26
L28         160 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27
L29           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND ?TUBERCUL?
L30           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  28164-57-0/BI
L31           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28(L)(?MEDIC? OR ?PHARM? OR
                ?DRUG? OR THERAP? OR MYCOBACTERIUM)
L32           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 NOT L29
L33             SEL  PLU=ON  L30 1- CHEM :       4 TERMS
L34          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33
L35           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND ?TUBERCU?
L36           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 NOT (L29 OR L32)


=>
=>

=> d ibi abs hitstr l36 1
'IBI' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'
ENTER DISPLAY FORMAT (BIB):end

=> d ibib abs hitstr l36 1

L36  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2003:89327  HCAPLUS
TITLE:                   Antimycobacterial activity of diospyrin
                         derivatives and a structural analogue of
                         diospyrin against Mycobacterium
                         tuberculosis in vitro
AUTHOR(S):               Lall, N.; Das Sarma, M.; Hazra, B.; Meyer, J. J. M.
CORPORATE SOURCE:        Department of Botany, University of Pretoria,
                         Pretoria, 0002, S. Afr.
SOURCE:                  Journal of Antimicrobial Chemotherapy (2003), 51(2),
                         435-438
                         CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER:               Oxford University Press
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Three derivs. and one structural analog of diospyrin were
     synthesized and investigated for their inhibitory activity against
     Mycobacterium tuberculosis employing the rapid radiometric
     method in vitro.  A novel aminoacetate deriv. was found to be more active
     than the parent compd., the MICs being 50 and 100 mg/L, resp., for a
     drug-susceptible strain, H37Rv, of M. tuberculosis.  This deriv.
     also exhibited an MIC of 50 mg/L for a few multidrug-resistant strains of
     M. tuberculosis.  The other two derivs. and the analog did not
     show any significant antimycobacterial activity at the highest concn. (100
     mg/L) tested.
REFERENCE COUNT:         9     THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
=> d stat que
L24             STR
```



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L25          875 SEA FILE=REGISTRY SSS FUL L24
L26              STR
```



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L27          112 SEA FILE=REGISTRY SUB=L25 SSS FUL L26
L28          160 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27
L29            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND ?TUBERCUL?
L30            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  28164-57-0/BI
L31            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28(L)(?MEDIC? OR ?PHARM? OR
                 ?DRUG? OR THERAP? OR MYCOBACTERIUM)
L32            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 NOT L29
L33              SEL  PLU=ON  L30 1- CHEM :        4 TERMS
L34           68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33
L35            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND ?TUBERCU?
L36            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 NOT (L29 OR L32)
L40            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND (?MYCOBACT? OR
                 ANTIBACT?)
L41            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 NOT (L29 OR L32 OR L36)
```

=>
=>

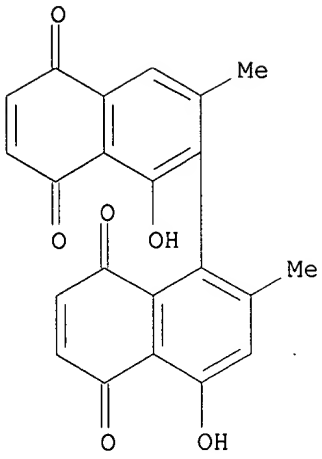
=> d ibib abs hitstr l41 1-3

L41 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:243113 HCAPLUS
DOCUMENT NUMBER: 133:28470
TITLE: **Antibacterial** activity of diospyrin, isodiospyrin and bisisodiospyrin from the root of Diospyros piscatoria (Gurke) (Ebenaceae)
AUTHOR(S): Adeniyi, B. A.; Fong, H. H. S.; Pezzuto, J. M.; Luyengi, L.; Odelola, H. A.
CORPORATE SOURCE: Department of Pharmaceutical Microbiology and Clinical Pharmacy, College of Medicine, University of Ibadan, Ibadan, Nigeria
SOURCE: Phytotherapy Research (2000), 14(2), 112-117
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

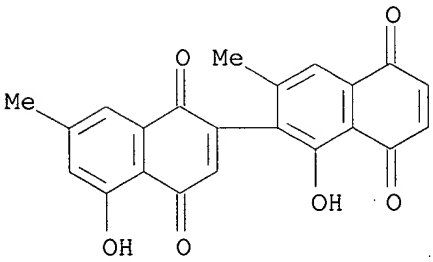
AB Two dimeric naphthoquinones, diospyrin and isodiospyrin, isolated from the root of Diospyros piscatoria (Gurke), a common ingredient in several folk medicines, have been shown to have a broad spectrum of **antibacterial** activity. The min. inhibitory concns. (MICs) of diospyrin against Streptococcus pyogenes ATCC 12344 and Streptococcus pneumoniae ATCC 33400 ranged from 1.56 to 50 .mu.g/mL. While those against Salmonella choleraesuis serotype typhi (S. typhi), ATCC 6539 and **Mycobacterium** chelonae ATCC 19977 were between 25 and 100 .mu.g/mL. Isodiospyrin was more active than its racemic isomer diospyrin. The MICs against Gram-pos. bacteria ranged from 0.78 to 50 .mu.g/mL. While those against Pseudomonas aeruginosa ATCC 15443 and S. typhi ranged from 50 to 100 .mu.g/mL. The MIC for M. chelonae was between 6.25 and 25 .mu.g/mL. MICs were found to increase with the concn. of cells used for the inoculum. The MICs for Bacillus subtilis ATCC 6633 increased up to the highest concn. of cells tested. The same phenomenon was obsd. on M. chelonae, but with better effect in the latter. The kinetics of bacteria studies against both B. subtilis and M. chelonae increases with increasing concn. of isodiospyrin tested. Two tetrameric forms of plumbagin were isolated. The naphthoquinone bisisodiospyrin, gave MIC values between 300 and 400 .mu.g/mL. The second, as yet unidentified tetramer, was not active at 500 .mu.g/mL.

IT **20175-84-2P**, Isodiospyrin **28164-57-0P**, Diospyrin
30276-87-0P, Bisisodiospyrin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(**antibacterial** activity of diospyrin, isodiospyrin, and bisisodiospyrin from the root of Diospyros piscatoria)

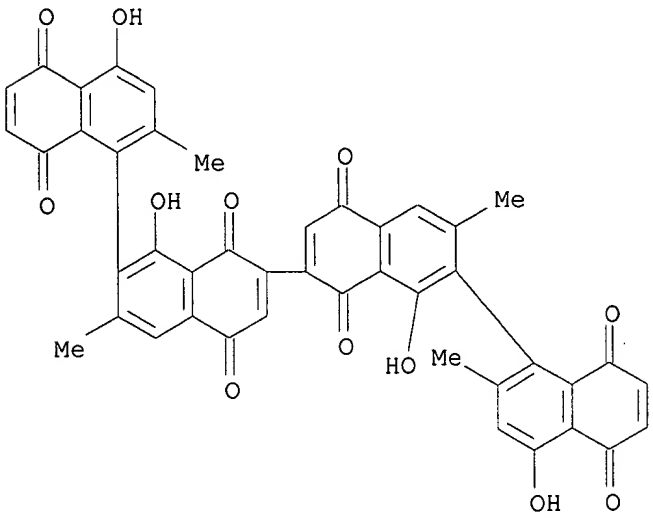
RN 20175-84-2 HCAPLUS
CN [1,2'-Binaphthalene]-5,5',8,8'-tetrone, 1',4-dihydroxy-2,3'-dimethyl-, (1R)- (9CI) (CA INDEX NAME)



RN 28164-57-0 HCAPLUS
CN [2,2'-Binaphthalene]-1,4,5',8'-tetrone, 1',5-dihydroxy-3',7-dimethyl- (8CI, 9CI) (CA INDEX NAME)

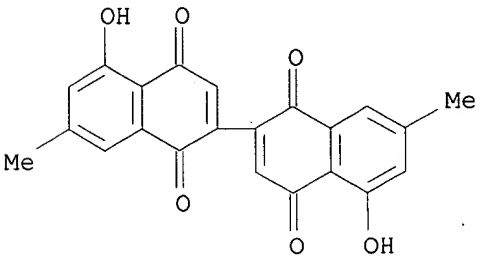


RN 30276-87-0 HCAPLUS
CN [1,2':7',2'':7'',1'''-Quaternaphthalene]-1'',4'',5,5',5''',8,8',8'''-octone, 1',4,4''',8''-tetrahydroxy-2,2''',3',6''-tetramethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:430463 HCAPLUS
DOCUMENT NUMBER: 131:291097
TITLE: Constituents of Diospyros lolin, D. Maritima and D. Novoguinensis
AUTHOR(S): Khan, M. R.; Timi, D.
CORPORATE SOURCE: Department of Applied Sciences, Papua New Guinea University of Technology, Papua, Papua New Guinea
SOURCE: Fitoterapia (1999), 70(2), 194-196
CODEN: FTRPAE; ISSN: 0367-326X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Antibacterial** activity of 7-methyljuglone (I), plumbagin (II), and biramentaceone isolated from Diospyros species was studied. Only I and II showed **antibacterial** activity.
IT **24456-79-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(isolation and **antibacterial** activity of constituents of Diospyros)
RN 24456-79-9 HCAPLUS
CN [2,2'-Binaphthalene]-1,1',4,4'-tetrone, 5,5'-dihydroxy-7,7'-dimethyl- (8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1979:98323 HCAPLUS
DOCUMENT NUMBER: 90:98323
TITLE: Mutagenicity and **antibacterial** activity of mycotoxins produced by Penicillium islandicum Sopp and Penicillium rugulosum
AUTHOR(S): Stark, A. A.; Townsend, J. M.; Wogan, G. N.; Demain, A. L.; Manmade, A.; Ghosh, A. C.
CORPORATE SOURCE: Dep. Nutr. Food Sci., Massachusetts Inst. Technol., Cambridge, MA, USA
SOURCE: Journal of Environmental Pathology and Toxicology (1978), 2(2), 313-24
CODEN: JEPTDQ; ISSN: 0146-4779
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twelve mycotoxins produced by P. islandicum and P. rugulosum in solid-state fermn. on grains were purified and tested for mutagenicity and **antibacterial** activity in Salmonella/mammalian microsome assays. The mutations studied were reversions of histidine auxotrophs to prototrophy in strains TA98 and TA100 and forward mutations to 8-azaguanine resistance (8AGR) in strain TM677. Rubroskyrin [21884-47-9], (+)rugulosin [23537-16-8], lumiluteoskyrin [

22333-61-5] (a photoproduct of (-)luteoskyrin [21884-44-6]), and simatoxin [66257-36-1] (a new water-sol. metabolite of unknown structure) induced 8AGR mutations in strain TM677 but not histidine reversions in strains TA98 and TA100. Mutagenic potency was reduced by rat-liver microsomes. The carcinogens (-)luteoskyrin and cyclochlorotine [12663-46-6] were **antibacterial** but not mutagenic. (+)Rugulosin, rubroskyrin, lumiluteoskyrin, and high concns. of simotoxin were also **antibacterial**. **Antibacterial** activity but not mutagenicity was obsd. with pibasterol [66257-37-2] and skyrin [602-06-2]. Chrysophanol [481-74-3], islandicin [476-56-2], iridoskyrin [568-42-3], and emodin [518-82-1] were inactive as mutagens or as **antibacterial** agents.

IT **22333-61-5**
RL: BIOL (Biological study)
(of Penicillium islandicum and Penicillium rugulosum, bactericidal action and mutagenicity of)

RN 22333-61-5 HCAPLUS

CN 7,17:8,16-Dimethanocyclodeca[1,2-b:5,6-b']dinaphthalene-5,6,9,10,15,18-hexone, 7,8,16,17-tetrahydro-1,4,11,14,19,20-hexahydroxy-2,13-dimethyl- (8CI, 9CI) (CA INDEX NAME)